IN THE CLAIMS:

Please add the following claims.

42. The method of Claim 1, wherein said cell line is an Mpf cell line.

43. The method of Claim 6, wherein said cells are Mpf cells.

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44. The method of Claim 11, wherein said cell line is an Mpf cell line.

45. The method of Claim 16, wherein said cells are Mpf cells. --

REMARKS

Claims 1-21, 36-38 and 41 were examined. Claims 22-35, 39 and 40 have been withdrawn from consideration. Claims 42-45 have been added herein and are directed to the use of an Mpf cell lines or Mpf cells in the claimed methods. These claims do not add new matter. Accordingly, Claims 1-45 are pending. Reconsideration and allowance of this application are respectfully requested.

Rejection under 35 U.S.C. § 102

Claims 1, 3-6, 8-11, 13-21 and 36-38 have been rejected under 35 U.S.C. §102(e)[1] as allegedly anticipated by U.S. Patent No. 5,871,997 to Rother *et al.* (hereafter "Rother").

Claim 1 is directed to a method of preparing a stable, retroviral packaging cell line to produce human serum-resistant RVP. The relevant method step provides that one or

[1]In making the present rejection, the Examiner quoted 35 U.S.C. § 102(e) as forming the basis for this rejection but indicated that the rejection was made under 35 U.S.C. § 102(b). Since Rother was filed prior to Applicants' application and issued thereafter, Applicant will assume the rejection is under 35 U.S.C. § 102(e) unless the Examiner indicates otherwise.

more packaging vectors are introduced into a non-primate mammalian cell line that (1) exhibits substantially no hybridization to a Moloney-MLV retrovirus probe under stringent washing conditions and (2) is capable of producing human serum-resistant RVP. The remaining claims depend directly or indirectly from Claim 1, and thus each one includes these aspects of the cell line.

Rother does not disclose any such cell lines and therefore does not anticipate the invention as claimed. First, Rother is generally directed to cell lines which are of primate origin and which lack galactose alpha (1,3) galactosyl epitopes, *i.e.*, α-galactosyl negative cells (*see, e.g.*, Col. 9, Lines 19-23). Since these Rother cell lines are of primate origin they do not anticipate the cell lines in Claim 1 of the instant invention (which are non-primate mammalian cell lines). Moreover, all Rother cell lines must be α-galactosyl negative, and Rother teaches this is an important aspect of that invention. Since the presence or absence of α-galactosyl on the cells of the present invention is irrelevant, Rother teaches away from the instantly claimed invention.

Second, as the Examiner has pointed out, Rother discloses two α-galactosyl negative, non-primate cell lines as useful for producing human serum-resistant RVP: Chinese hamster ovary (CHO) and baby hamster kidney (BHK) cells (Col. 15). However, such cell lines contain endogenous retrovirus sequences which exhibit hybridization to a Moloney-MLV retrovirus probe under stringent washing conditions. While Rother is totally silent in this regard, the literature is not.

The following references establish that CHO cells have endogenous retrovirus sequences capable of hybridizing to a Moloney-MLV retrovirus probe under stringent washing conditions: Lie *et al.* (1994) Virology 68:7840-7849, Chinese Hamster Ovary Cells

Contain Transcriptionally Active Full-Length Type C Proviruses, *see, e.g.*, Page 7840, left column, second full paragraph and Page 7843, left column (hereafter "Lie"); and Anderson *et al.* (1991) Virology 181:305-311, Endogenous Origin of Defective Retroviruslike Particles From a Recombinant Chinese Hamster Ovary Cell Line, see, e.g., Page 306, right column, Page 308, right column (copies enclosed). Applicant notes that Moloney-MLV is a type C retrovirus.

BHK cells also contain endogenous retrovirus sequences which exhibit hybridization to a Moloney-MLV retrovirus probe under stringent washing conditions. The discussion of Fig. 6 of the Lie reference states "extended film exposure times did indicate that distantly-related [ML2G] sequences exist in BHK cells (data not shown)" (Pages 7845 and 7846). According to Lie, ML2G sequences are homologous to Moloney-MLV retrovirus sequences (Page 7843, left column).

Thus, both the BHK and CHO cell lines harbor endogenous retroviral sequences. Since Rother discloses only these cell lines or primate cell lines, Rother does not anticipate the present invention as provided in Claim 1 or any claim dependent thereon. Accordingly, this rejection under 35 U.S.C. § 102(e) is deemed overcome and withdrawal thereof respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph

Claims 2, 7, 12 and 41 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement because the Examiner indicated a deposit of the Mpf cell line is required if use of that cell line is claimed by ATCC accession number.

In point of fact, Applicant acquired the Mpf cell line directly from the American Type Culture Collection (ATCC) where it had already been deposited under ATCC Accession Number 1656-CRL. The ATCC description of the Mpf cell line designated as ATCC Accession Number 1656-CRL is submitted herewith as Exhibit A. Since the cell line is publicly available from the ATCC, further deposit is unnecessary. However, if the Examiner believes any other action is needed, he is invited to call the undersigned.

In addition, Applicant has added new Claims 42-45 directed to methods which use an Mpf cell line or Mpf cells. These claims do not recite the ATCC accession number and Applicant is entitled to such subject matter. Support for this subject matter is found throughout the specification, including at least at Page 1, Lines 9-15, and in original Claims 2, 7, 12 and 41.

Accordingly, this rejection is deemed obviated and withdrawal thereof is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1-21, 36-38 and 41 are rejected under 35 U.S.C. §112, second paragraph, as allegedly vague and indefinite for various reasons.

The Office Action indicates the phrase "... exhibits substantially no hybridization to a Moloney-MLV retrovirus probe under stringent hybridization conditions..." appears to be unclear.

Applicant respectfully disagrees and submits that the meaning of the phrase in question (*i.e.* "... exhibits substantially no hybridization to a Moloney-MLV retrovirus probe under stringent hybridization conditions . . .") is clear to the ordinarily-skilled artisan and that

such a person knows how to determine the extent of hybridization without resort to undue experimentation. Hybridization methods are well known (*see, e.g.*, Sambrook *et al.* (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, NY). Moreover, methods for screening a cell line for hybridization to endogenous retroviruses are discussed in the present specification, *e.g.*, at Page 7, Lines 20-31.

Applicant also submits that those skilled in the art know what is meant by the phrase "substantially no hybridization". As the Examiner is aware, the inclusion of relational words such as "substantially" does not render a claim fatally indefinite. The issue is whether one skilled in the art can determine from the specification and general knowledge in the art whether a particular product or process falls within the language of the claim. The the skilled artisan can distinguish between a) hybridization and b) substantially no hybridization on a Southern blot under a particular set of hybridization and stringency conditions. One thus ascertains the specificity of the hybridization and can readily decide whether a particular sample hybridizes to a given probe or whether it does not under the particular set of conditions. Since the subject matter here may not permit precise definition, using the term "substantially no hybridization" to indicate the absence of specific hybridization, does not render the claim indefinite nor does it obscure the metes and bounds of the claim. Applicant's terminology is commonly used and well understood in the art. Hence, these claims are neither vague nor indefinite.

Additionally, those skilled in the art can readily determine probes for use as a "Moloney-MLV retrovirus probe" since the sequences of Moloney-MLV retroviruses have long been known in the art (Schinnick et al. (1981) Nature 293:543-548, "Nucleotide Sequence of Moloney Murine Leukaemia Virus") and preparing such probes of suitable

length to detect an endogenous retrovirus sequence under stringent hybridization conditions is routine. Therefore, Applicant submits that further definition of this term is not required. A claim containing terms which are understandable to one of ordinary skill in the art when read in the context of general guidelines provided by the specification is not vague or indefinite. *In re Mattison*, 509 F.2d 563, 565, 184 USPQ 484, 486 (CCPA 1975).

Those skilled in the art recognize that the phrase "stringent conditions" refers to the conditions during washing after hybridization of two nucleic acids. The stringency of the wash conditions is determined by various factors including the composition of the nucleic acids, length of the nucleic acids, ionic strength of the wash solution and temperature. Moreover, the ordinarily skilled artisan knows these factors can be varied to generate conditions of either low or high stringency to achieve hybridization between sequences with particular amounts of sequence homology. As is well known, high stringency wash conditions allows hybridization of highly homologous sequences. Sambrook *et al.* provides ample details on conducting hybridization and determining the stringency conditions needed for washing the hybrids for a given probe.

The Examiner also has indicated that Claims 1, 6 and 11 are vague in the recitation of the phrase "capable of ..." The "capable of" language further defines particular characteristics of the cells as recited in the claims. For example, the skilled artisan understands that cells "capable of producing human-serum resistant RVP" have the ability, *i.e.*, the requisite cellular properties, to produce the aforementioned RVP. Moreover, this can be readily measured using methods taught in the specification or routinely available in the art. Again the metes and bounds of these claims are clear: either the cell line can or can not

produce the required RVP and the skilled artisan has the tools and knowledge to make that determination without undue experimentation.

Accordingly, Applicants believe that the claims are definite as drawn, that this rejection under 35 U.S.C. §112, second paragraph is obviated and should be withdrawn.

Conclusion

It is believed that the present application is in a condition for allowance which action is earnestly solicited. If the Examiner has any questions, he is invited to contact the undersigned to discuss this application.

Respectfully submitted,

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